Table S5. Genes with the most significant expression changes among each subtype of immune cells.

Gene	Sepsis Average (log2)	Control Average (log2)	Fold Change	FDR P-value	Function
Neutrophils					
Vanin 2 (VNN2)	7.25	4.08	9.02	5.49E-08	Encodes proteins associated with hematopoietic cell migration and oxidative stress response (1).
Vacuole Membrane Protein 1 (VMP1)	7.39	5.53	3.63	2.78E-06	Transmembrane protein playing a role in autophagy regulation (2).
Formyl Peptide Receptor 2 (FPR2)	5.34	3.6	3.35	8.71E-06	Diverse pattern recognition receptor involved in organ-protection (3). Potential therapeutic target for leukocyte-induced inflammatory diseases like sepsis (4).
Exportin 6 (XPO6)	6.84	5.14	3.25	3.62E-06	Mediates export of proteins through the nuclear envelope (5).
Chemokine (C-X-C motif) Receptor 1 (CXCR1)	6.47	4.94	2.89	6.07E-05	Dominant cell surface receptor for PMNs during sepsis (6). Blockade of CXCR1/2 ameliorates LPS-induced ALI (7).
Prokineticin 2 (PROK2)	7.1	5.58	2.86	4.13E-06	Protein associated with various biological functions such as circadian rhythms and immunoinflammatory processes (8), upregulated in sepsis models (9).
Fc-Gamma Receptor IIIb (CD16b) (FCGR3B)	7.01	5.54	2.77	5.00E-04	Regulates IgG complexes in peripheral circulation, and the release of TNF during inflammation of endothelial cells (10).
Solute Carrier Family 25, Member 37 (SLC25A37)	6.64	5.44	2.29	9.10E-06	Mitochondrial iron transporter localized on inner membrane.
Chitobiase (CTBS)	4.78	3.69	2.13	1.67E-05	Lysosomal glycosidase used for degradation.
Free Fatty Acid Receptor 2 (FFAR2)	5.74	4.79	1.93	9.00E-04	Upregulated expression during infection in signal transduction pathways, apoptosis, and immune cell activation (11).
Family with sequence similarity 53, member C (FAM53C)	5.31	5.24	1.05	0.3658	Protein binding to regulators of cell proliferation.
tRNA Splicing Endonuclease Subunit 34 (TSEN34)	5.59	5.58	1	0.1899	Catalytic subunits of tRNA splicing endonuclease, involved in protein processing.
Adenosine Monophosphate Deaminase 2 (AMPD2)	5.89	5.9	-1	0.7418	Important deaminase for purine biosynthesis, converting AMP to IMP.
Ankyrin Repeat and BTB Domain Containing 1 (ABTB1)	6.22	6.23	-1.01	0.8856	Coding region involved in protein to protein interactions.
Metallophosphoesterase 1 (MPPE1)	5.1	5.2	-1.07	0.0219	Protein with hydrolase activity involved in GPI-anchor protein transport.
Polyhomeotic Homolog 2 (PHC2)	5.9	6.01	-1.08	0.0063	No specific function in human cells has been determined.

CKLF-like MARVEL Transmembrane domain containing 2 (CMTM2)	4.74	4.93	-1.14	0.1157	Encodes molecules linking chemokines and transmembrane 4 family signaling.
Chemokine (C-C motif) Receptor 3 (CCR3)	2.84	3.18	-1.26	6.00E-04	Regulates inflammatory response to prevent hyperactivity (12). Modulates Th2 proliferation and low expression correlates with decreased survival (13).
Charcot-Leyden Crystal galectin (CLC)	3.01	3.44	-1.35	0.0137	Lysophospholipase, able to bind IgE, involved in inflammation and myeloid cell activity (14).
Tetraspanin 16 (TSPAN16)	3.72	4.17	-1.37	3.89E-08	Cell-surface proteins involved in signal transduction, cellular development, mobility, and adhesion in hematopoietic cells.
Monocytes					
ATPase type 13A3 (ATP13A3)	6.46	4.13	5	1.78E-07	Important for transmembrane cation transport .
Interleukin 1 Beta (IL1B)	7.62	5.34	4.84	2.00E-04	Pro-inflammatory cytokine upregulated during sepsis (15). Critical role in coagulation pathways influencing onset of septic shock (16).
Nuclear Enriched Abundant Transcript 1 (NEAT1)	8.72	6.73	3.96	1.18E-06	Upregulates inflammatory cytokines; positively correlated with risk, severity and poor prognosis in sepsis patients (17). Potential therapeutic target for sepsis-induced AKI (18).
6-Phosphofructo-2-kinase/Fructose-2,6-Biphosphatase 3 (PFKFB3)	8.81	6.83	3.96	6.47E-09	Important glycolytic enzyme; inhibitors found to have therapeutic potential for sepsis-induced ALI by reducing lung cell inflammation and apoptosis (19).
Cytochrome B-245, Beta polypeptide (CYBB)	7.01	5.07	3.84	5.00E-04	Component of oxidase system in phagocytes; role in regulation of ROS production during sepsis, known to cause cell death and vascular inflammation (20, 21).
Plasminogen Activator, Urokinase Receptor (PLAUR)	7.65	5.96	3.23	4.85E-05	Multifunctional protein important during systemic inflammation, urosepsis, and liver failure; potential diagnostic marker for sepsis and cirrhosis (22, 23).
Solute Carrier Family 3 Member 2 (SLC3A2)	7.08	5.74	2.53	1.95E-06	Amino acid membrane transporter upregulated during bacterial infection (24).
Versican (VCAN)	5.58	4.31	2.41	5.69E-05	Upregulated expression during sepsis systemic infection, mediating endothelial tissue repair; associated with increased survival (25).
Cathepsin D (CTSD)	8.94	7.7	2.36	5.94E-05	Autolysosomal protein released during cell degradation induced during endotoxemia (26, 27).
Peptidylprolyl Isomerase F (PPIF)	7.04	5.89	2.21	8.00E-04	Pore in inner mitochondrial membrane playing a role in apoptosis and cell death.
Ribulose-5-Phosphate-3-Epimerase Like 1 (RPEL1)	2.51	2.68	-1.13	5.00E-04	Encodes enzyme important for carbon metabolism and NADPH production to manage intracellular oxidation.
PML-RARA Regulated Adaptor Molecule 1(PRAM1)	5.98	6.21	-1.17	4.95E-05	Adaptor protein for T cell signaling, regulated during myeloid cell production.
CD1D molecule (CD1D)	5.22	5.46	-1.18	1.46E-05	Antigen-presenting glycoprotein modulating NKT cell activity and downregulating effector T cell immunity (28, 29).

Interleukin 36, Gamma (IL36G)	3.19	3.43	-1.18	0.0028	Member of IL1 family, stimulating expression of cytokines in keratinocytes.
Pro-Platelet Basic Protein (PPBP)	3.01	3.25	-1.18	0.8844	Growth factor activating innate immune response cells; involved in platelet hyperreactivity during sepsis, increasing risk for vascular damage (30).
Serpin Peptidase Inhibitor, family B, member 7 (SERPINB7)	3.46	3.79	-1.26	2.37E-06	Functions as a protease inhibitor upregulated during IgA nephropathy.
Interleukin 19 (IL19)	3.92	4.27	-1.28	0.0022	Pro-inflammatory cytokine regulating epithelial cell survival and PMN chemotaxis, associated with lung and liver injury during endotoxemia (31).
Chemokine (C-C motif) Ligand 24 (CCL24)	4.66	5.04	-1.29	1.13E-06	Anti-inflammatory chemokine important for T cell activation; decreased expression during sepsis (32).
Long Intergenic Non-Protein Coding RNA 158 (LINC00158)	3.08	3.48	-1.32	9.49E-08	Non-coding RNA gene.
Interleukin 24 (IL24)	3.66	4.06	-1.33	3.14E-07	IL10 family cytokine; associated with increased risk of complications from cardiac surgery in septic shock patients (33).
B Cells					
Kruppel-like Factor 6 (KLF6)	8.22	6.13	4.24	8.26E-10	Molecular switch between pro-inflammation and inhibition for vascular homeostasis (34).
SEC62 Homolog, Preprotein Translocation Factor (SEC62)	6.81	5.33	2.8	4.71E-08	Dimeric complex on human ER membrane important for polypeptide translocation (35).
Heat Shock Protein 90kda Beta 1 (HSP90B1)	7.64	6.23	2.66	9.21E-06	Protein transport chaperone assisting in pro-inflammatory conditions (36) with a role in sepsis-induced acute lung injury (37).
Mannosidase, Alpha, Class 1A, Member 1 (MAN1A1)	5.95	4.63	2.5	1.12E-08	Golgi Type II Transmembrane protein which hydrolyzes mannose residues; role in cell adhesion (38).
Ezrin (EZR)	8.28	7.11	2.26	3.49E-07	Peripheral membrane protein with key role in cell migration and proliferation (39).
Translocation Associated Membrane Protein 1 (TRAM1)	6.13	5.05	2.12	3.88E-06	Highly important ER glycoprotein for translocation of significant proteins such as B-lactamase and Preprolactin (40).
Elongation Factor, RNA Polymerase II, 2 (ELL2)	5.42	4.37	2.08	8.33E-05	Important for regulation of transcriptional elongation by RNA Pol II with both promoter-specific and independent sequences (41).
Ubiquitin-Conjugating Enzyme E2, J1 (UBE2J1)	6.8	5.75	2.06	2.42E-07	ER-membrane enzyme important for quality control degradation of proteins with ubiquitin-proteasome system (42).
SEC24 Homolog A, COPII Coat Complex Component (SEC24A)	5.04	4	2.05	4.93E-06	Role in sorting and processing of secretory proteins transported from the ER (43).
Ubiquitin Conjugating Enzyme E2, G1 (UBE2G1)	6.03	5.02	2.01	9.39E-07	ER-membrane enzyme important for degradation of muscle-specific proteins (44).
Tumor Necrosis Factor Receptor Superfamily, Member 13C (TNFRSF13C)	5.85	6.16	-1.24	4.79E-07	Principal membrane receptor for mature B-cell survival; Involved in pathogenesis of autoimmune diseases (45).
G Protein-Coupled Receptor, Class C, Group 5, Member D (GPRC5D)	4.16	4.51	-1.27	4.41E-05	Protein receptor found to have increased expression in kidney, pancreas and prostate (46).

Tumor Necrosis Factor Receptor Superfamily, Member 17 (TNFRSF17)	2.53	2.88	-1.27	1.24E-06	Receptor highly expressed on mature B lymphocytes, plays a role in autoimmune response, B cell proliferation and cell survival signaling (47).
FC Receptor-Like 2 (FCRL2)	2.9	3.28	-1.3	3.58E-07	Immunoglobulin receptor important for autoimmunity signaling. Observed role in chronic lymphocytic leukemia (48).
Prepronociceptin (PNOC)	4.84	5.24	-1.31	1.79E-07	PNOC associated with higher mRNA levels in sepsis; Precursor for nociceptin, involved in hypotension and microvascular inflammation, which contribute to pathogenesis (49).
FC Receptor-Like 5 (FCRL5)	3.71	4.13	-1.34	2.33E-08	Immunoglobulin receptor involved in B cell proliferation and lymphomagenesis (50). Surface marker of tissue-like memory B cells upregulating T-bet expression during infection (51).
NLR family, Pyrin domain containing 7 (NLRP7)	3.9	4.34	-1.36	1.42E-07	Regulator of inflammasomes, upregulated during inflammation and host immune system activation (52).
POU class 2 Associating Factor 1; B-cell translocation gene 4 (POU2AF1)	2.94	3.4	-1.37	9.48E-09	B-cell translocation gene; Transcription cofactor heavily expressed on lymphocytes and airways basal stem cells, implicated in immune response (53).
FC Receptor-Like A (FCRLA)	3.8	4.28	-1.4	1.67E-09	Intracellular receptor involved in Ig assembly by B cells during immune response to infection (54).
PRE-B Lymphocyte Protein 3 (VPREB3)	5.15	5.79	-1.56	3.43E-10	Upregulated during B cell maturation, commonly found in bone marrow and lymphoid tissue with significant role in immunological response. Also found in adrenal cortex, affected by aldosterone fluctuations (55).
Dendritic Cells					
Major Histocompatibility complex, class II, DR Beta 4 (HLA-DRB4)	6.83	5.87	1.94	0.0019	Key player in immune system antigen presentation at the cell membrane (56).
Nuclear Receptor subfamily 4, group A, member 3 (NR4A3)	5.25	4.5	1.68	7.00E-04	Encodes transcriptional activator for steroid-thyroid hormone-retinoid receptor.
MOB kinase activator 1B (MOB1B)	4.15	3.73	1.34	2.49E-05	Protein Kinase important for spindle formation during mitosis.
Heme Oxygenase 1 (HMOX1)	6.72	6.32	1.32	0.0031	Upregulated during oxidative stress occurring in the brain during infection (57). Indicator of mitochondrial dysfunction during LPS-induced sepsis; may reduce risk of ALI (58).
MX dynamin-like GTPase 1 (MX1)	5.36	4.99	1.29	0.0141	Encodes GTPase protein involved in IFN-mediated response to infection, enhancing innate immunity (59, 60).
5-Nucleotidase, Cytosolic IIIA (NT5C3A)	3.47	3.1	1.29	2.00E-04	Encodes enzyme for dephosphorylation of 5'-monophosphates.
Biogenesis of Lysosomal Organelles Complex-1, Subunit 6, pallidin (BLOC1S6)	4.62	4.29	1.26	1.68E-06	Protein for intracellular vesicle transport and production of lysosome-related organelles like platelet granules.
TRAF-type zinc Finger Domain containing 1 (TRAFD1)	5.34	5.03	1.24	3.30E-05	Negative feedback regulator for hyperreactive innate immune response during infection.
G-Rich RNA Sequence binding Factor 1 (GRSF1)	5.15	4.86	1.22	8.00E-04	Cytoplasmic protein preferentially binding RNAs with G-rich element, often in viral mRNA.

Interferon Induced, with Helicase C domain 1 (IFIH1)	4.21	3.93	1.21	0.0449	Important role in host innate immune response to systemic infection (61).
Arachidonate 15-Lipoxygenase (ALOX15)	4.61	4.96	-1.27	2.49E-06	Encodes enzyme that generates lipid mediators, important in inflammation and immune response.
Sialic acid binding IG-like Lectin 1, Sialoadhesin (SIGLEC1)	5.49	5.85	-1.28	3.98E-08	Type I transmembrane protein on macrophages important for cell-cell adhesion.
ADAM metallopeptidase domain 12 (ADAM12)	4.29	4.67	-1.3	7.02E-08	Multipurpose enzyme for cell/matrix interactions during fetal, muscle, and neuron development.
Ubiquitin Specific Peptidase 18 (USP18)	4.73	5.1	-1.3	6.34E-08	Interacts with interferon-stimulated genes for covalent attachment to antigens, leading to macrophage activation (62).
CD1B molecule (CD1B)	2.92	3.31	-1.31	2.67E-08	Glycoprotein important for antigen presentation to T cells.
Solute Carrier Organic anion transporter family, member 5A1 (SLCO5A1)	3.7	4.09	-1.31	5.73E-08	Transmembrane protein important for anion transport in the cell.
Cytokine Receptor-Like Factor 2 (CRLF2)	4.75	5.16	-1.32	1.30E-08	Receptor for TSLP, upregulated on CD14+ monocytes during LPS-induced sepsis; plays a role in myeloid cell proliferation pathway (63).
Dendritic Cell-Associated Nuclear Protein (DCANP1)	4.04	4.43	-1.32	4.91E-06	Protein expressed in DCs to activate naïve T cells, initiating adaptive immune response.
Tweety Family member 2 (TTYH2)	5.55	5.94	-1.32	7.01E-10	Encodes chloride anion channels found to be associated with kidney tumors.
CD1A molecule (CD1A)	4.71	5.3	-1.51	1.99E-11	Antigen-presenting protein, under sepsis conditions it enhances regulatory T cell cytokines modulating immuno-inflammatory response (64).
NK Cells					
Influenza Virus NS1A Binding Protein (IVNS1ABP)	7.35	4.61	6.68	1.11E-06	Involved in pre-mRNA splicing and other molecular cell functions.
Chloride Intracellular Channel 3 (CLIC3)	5.53	5.53	1	0.2792	Chloride intracellular channel, stabilizes membrane potential, ph, and cell volume.
Carbohydrate Sulfotransferase 12 (CHST12)	6.24	6.27	-1.02	0.2805	Localized in Golgi membrane, forms a proteoglycan present in cell surface, matrix, and cartilage.
Yippee Like 1 (YPEL1)	4.68	4.77	-1.07	0.0216	Localized to nucleolus and centrosome, associated with cellular division.
Killer Cell Lectin-Like Receptor F1 (KLRF1)	1.84	1.99	-1.11	0.0247	Expressed on all NK cells, mediating cytokine release and cytotoxicity.
Prostaglandin D2 Receptor (PTGDR)	4.76	4.98	-1.16	5.37E-05	Transmembrane protein regulating allergic inflammatory response.
CD244 molecule (CD244)	3.99	4.25	-1.19	2.32E-06	Anti-inflammatory receptor 2B4 on NK cells and memory $CD8^+$ T cells, responsible for immune dysregulation and mortality risk in sepsis (65).
Killer Cell Immunoglobulin-Like Receptor, 3 Domains, Long cytoplasmic tail 2 (KIR3DL2)	5.06	5.62	-1.48	1.58E-09	Transmembrane glycoprotein transducing inhibitory signals to NK cells and some T cells, associated with regulating immune response to infection.

Killer Cell Immunoglobulin-Like Receptor, 3 Domains, Long/Short cytoplasmic tail 1 (KIR3DL1/S1)	4.89	5.51	-1.53	1.05E-09	Part of complex activation system for NK cells and T cells through interaction with HLA molecules, associated with many disease processes (66).
T Cells					
DNAJ (Hsp40) Family member B1 (DNAJB1)	7.43	6.2	2.34	1.63E-06	Molecular chaperone stimulating Hsp70 ATPase activity for protein assembly.
Solute Carrier Family 25 Member 3 (SLC25A3)	6.27	5.38	1.85	5.89E-09	Phosphate transporter into mitochondrial matrix through proton exchange.
Nedd4 Family Interacting Protein2 (NDFIP2)	4.53	4.25	1.22	0.0012	Found to have signal transducing activity, with some regulation of EGFR signaling.
H2A Histone Family, member X (H2AFX)	6.03	5.86	1.13	0.0498	Replication-independent core histone molecule for transcript generation.
Ubiquitin-Conjugating Enzyme E2S (UBE2S)	6.17	5.99	1.13	5.00E-04	Important ubiquitin carrier enzyme, also playing a role in cell progression through mitosis.
Leptin Receptor Overlapping Transcript-Like 1 (LEPROTL1)	4.73	4.57	1.12	0.0016	Protein-coding gene, no specific function yet found.
Phosphoribosylaminoimidazole Carboxylase and Phosphoribosylaminoimidazolesuccinocarboxamide Synthase (PAICS)	4.51	4.39	1.09	0.0828	Bifunctional enzyme important for purine biosynthesis.
EGL-9 family hypoxia-inducible factor 3 (EGLN3)	4.89	4.82	1.05	0.0748	Encodes proteins important for oxidative stress response during infection (67), overexpression during sepsis reverses cytokine/chemokine activity (68).
Cyclin B1 (CCNB1)	3.28	3.24	1.02	0.6852	Regulator of mitosis in cell cycle; potential therapeutic target for sepsis-induced ARDS (69).
HAUS Augmin-like Complex Subunit 1 (HAUS1)	3.34	3.3	1.02	0.63	Critical complex for increasing microtubule generation during mitosis.
Interleukin 22 (IL22)	3.29	3.64	-1.27	1.00E-04	Pro-inflammatory cytokine, promoting intestinal epithelial regeneration (70). Found to limit heme availability, suppressing bacterial growth during systemic infection (71).
CD6 molecule (CD6)	5.54	5.9	-1.28	6.68E-08	Lymphocyte receptor able to bind PAMPs during infection and trigger MAPK cascade; potential target to prevent septic shock (72).
Carboxypeptidase O (CPO)	3.39	3.76	-1.29	2.00E-06	Important enzyme on the ER, cleaving acidic and polar AAs, and small lipid droplets (73).
Interleukin 9 (IL9)	3.78	4.15	-1.29	8.39E-09	Regulator cytokine of hematopoietic cells, important for resolution of inflammation (74).
Inducible T-cell Co-stimulator (ICOS)	2.31	2.68	-1.3	1.08E-05	Important molecule for immunological cell signaling and proliferation of T cells; inverse association with SOFA and mortality in sepsis (75).
Macrophage Stimulating 1 (MST1)	5.81	6.2	-1.31	1.08E-07	Kinase activity regulating ROS production and bactericidal activity in phagocytes (76). Upregulation associated with sepsis-induced myocardial injury (77).

CD3D molecule, delta (CD3-TCR complex) (CD3D)	4.03	4.43	-1.33	6.18E-08	Important role in immune signal transduction and T cell proliferation; inversely associated with SOFA and mortality (75), and good predictor of postoperative sepsis (78).
Cytotoxic T-Lymphocyte-Associated Protein 4 (CTLA4)	4.63	5.06	-1.34	4.16E-07	Negatively regulates T cell activation during sepsis; upregulation diminishes response to antigens (79). Inhibition reduces TSST-1 mortality risk (80).
Interleukin 17F (IL17F)	3.26	3.69	-1.34	2.49E-08	Cytokine for innate immune response to bacteria (81). No crucial role in LPS-induced endotoxic shock compared to IL17A (82).
Lymphocyte-Activation Gene 3 (LAG3)	4.88	5.31	-1.34	7.15E-09	Suppresses T-cell signaling, significantly upregulated in HIV positive sepsis patients, marker of “immune exhaustion” (83).

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